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Metabolic features of chronic fatigue syndrome (CFS)

Metabolic features of chronic fatigue syndrome is a groundbreaking paper by Naviaux Lab on the Metabolic study of Chronic Fatigue Syndrome (CFS) patients which demonstrates significant blood chemical signatures. It was published in Proceedings of the National Academy of Sciences of the Unites Stats of America (PNAS) on August 24, 2016. This paper is open data and open access.

Excerpt:

Chronic fatigue syndrome is a multisystem disease that causes long-term pain and disability. It is difficult to diagnose because of its protean symptoms and the lack of a diagnostic laboratory test. We report that targeted, broad-spectrum metabolomics of plasma not only revealed a characteristic chemical signature but also revealed an unexpected underlying biology. Metabolomics showed that chronic fatigue syndrome is a highly concerted hypometabolic response to environmental stress that traces to mitochondria and was similar to the classically studied developmental state of dauer. This discovery opens a fresh path for the rational development of new therapeutics and identifies metabolomics as a powerful tool to identify the chemical differences that contribute to health and disease.

Thirteen questions answered on Metabolic features of chronic fatigue syndrome

SUMMARY: Dr. Robert Naviaux answers questions about his findings. Original Q & A: 1-6 ,Updated Q & A: 1.1 & 7-12

1. CFS is a real illness with blood chemical signature and is Metabolic, not all in the mind

1.1 Profound personal loss, grief, depression, fear, chronic pain, anxiety, and PTSD all cause chemical changes in the blood that we can measure with metabolomics. The science behind the expanded CFS metabolomics study demands that we ask both CFS subjects and normal controls about psychological trauma to see if this can increase the susceptibility to CFS later in life, and to see how previous trauma might influence current metabolomics.

2. Cell danger response (CDR) does not switch off and results in a "siege metabolism"

3. People do not hibernate, CFS has a metabolic signature of dauer

4. Men and women are different in this disease, not related to testosterone or estrogen

5. Epigenetics and DNA Methylation pathways relevant to this disease

6. This paper is not related to treatment although Metabolomics will be relevant to any clinical trial of CFS

7. Dr. Naviaux is in agreement with Ron Davis that chronic use of antibiotics can inhibit mitochondrial function. Therefore long term use of antibiotics with no evidence of an active infection are doing more harm than good.

8. Mitochondria have two main jobs in the cell - energy metabolism and cellular defense and one can be overactive at the expense of the other. Mitochondrial cannot perform both energy and defense (against colds, flu, etc.) at 100% all the time.

9. Does the fact that some antibiotics can inhibit mitochondria mean that treatments for Lyme disease that last too long might actually convert an acute Lyme infection to a chronic post-Lyme syndrome and chronic fatigue syndrome? Yes.

10. Are there mito-cocktails or supplements that can help until scientists have more definitive treatments? There is no simple answer. Flares and jolts to the body systems of CFS patients can occur with mito-cocktails. Start low, and go slow as some doses of B6 and magnesium can cause heart palpitations.

11. By giving antivirals, doctors are not just inhibiting viruses, they are also inhibiting many host cell metabolic functions. Sometimes the inhibition of host cell functions can attenuate ME/CFS symptoms for a time, but in other cases, using potent antiviral drugs inhibits mitochondrial and methylation reactions and can delay a full recovery from ME/CFS.

12. Our studies show that metabolism might be the final common denominator for ME/CFS. It is important to remember that “diet” and “metabolism” are not the same. Diet is what we eat. Metabolism is the performance state of the matrix—the dynamic state of flow in the network that constitutes all the biochemical reactions that our cells use to conduct the business of life.

Viruses and CFS: Statements by Ron Davis and Bob Naviaux

Below is a portion of their statements.

Excerpts:

Ron Davis: "There is a great deal of evidence that a variety of viruses can initiate ME/CFS, but it is less clear that a virus is involved in sustaining the disease. However, some patients may have a continuous problem with viruses, especially those viruses we always carry like EBV and HHV6.

These viruses are usually kept in check by the immune system. Any suppression of the immune system can cause reactivation of these viruses (e.g., shingles). It is possible (we have new supporting data on this) that the immune system is somewhat impaired in ME/CFS, which will make it difficult to keep these viruses suppressed. If we can find the cause of this disease and cure it, this virus problem should go away."

Bob Naviaux: Question- Many ME/CFS experts have improved the symptoms in some patients by treating with antivirals and Ampligen (polyIC double stranded RNA). I think this proves that ongoing viral infections are causing our symptoms. It is not merely “tired patients” who are stuck in a lowered metabolic state because of a past trigger (which now is gone).

"First of all, it is important that people actually read our paper first before drawing conclusions from news reports and blogs and criticizing something that we never said. I have seen a number of generalizations starting to appear in blogs and reports by journalists in even good newspapers and magazines that are starting to drift too far afield from the actual science in our paper.

We devoted a section of the paper to this and related questions about infections. The section title was, “A Homogeneous Metabolic Response to Heterogeneous Triggers”. It concluded with the sentence, “Despite the heterogeneity of triggers, the cellular response to these environmental stressors in patients who developed CFS was homogeneous and statistically robust.” As background for this conclusion, I recommend reading our paper on this topic entitled, “Metabolic features of the cell danger response” (PMID 23981537).

Second, many people do not understand that the first response our body mounts against a viral, bacterial, or any kind of infection is metabolic. Yes, our chemistry is our first line of defense. Our chemistry reflects our instantaneous state of

health. Innate immunity is coordinated by mitochondria and is an essential first step in developing adaptive immunity to any infectious agent. Without innate immunity there can be no antibodies and no NK cell activation, no mast cell activation, and no T cell mediated immunity.

In addition, all antivirals have metabolic effects that have nothing to do with inhibiting viral DNA or RNA synthesis directly. Many antiviral drugs inhibit the key metabolic enzyme SAdenosylhomocysteine Hydrolase (SAHH). Inhibition of SAHH causes an increase in intracellular SAH levels. SAH is a potent inhibitor of DNA, RNA, protein, and small molecule methylation. This affects both viral and host cell epigenetics, gene expression, mRNA translation, and protein stability."

Analysis of Metabolic features of chronic fatigue syndrome

Excerpt:

For those who are wondering at the results and their implications, Naviaux's study in a nutshell states that the cells of ME patients are in a sort of protective hibernation, limiting their consumption of resources and engaging in a hypometabolic state as a response to infection or other stressors. By examining patients' metabolites in detail, it was found that this degree of protective hibernation correlates directly to clinical severity.

Naviaux also posits that cells in ME/CFS are cells under enormous stress, for which they create a series of defenses, metaphorically installing a superior lock and alarm system and hiding all the valuables. However, some pathogens know the code to get in, and when the resources are hidden, the host can't use them, either. Both of these aspects of this mode of cellular defense have profound implications for symptomology.

Health Rising - The Core Problem in Chronic Fatigue Syndrome Identified? Naviaux's Metabolomics Study Breaks Fresh Ground

Excerpt:

Naviaux believes the mitochondria are able to sense every kind of danger – from pathogens to pH changes to toxic elements from pesticides, heavy metals, etc. to inflammation. They sense trouble in the form of an infection when they detect a drop in voltage caused by the diversion of electrons (NADH / NADPH) to make viral components or respond to a broad variety of toxins.

In the cell danger response (CDR) the mitochondria respond instantaneously to that loss by decreasing their oxygen consumption – thus thwarting pathogens from using the building blocks of the cell to replicate. Because the oxygen is no longer being used, it builds up in the cells causing a oxidatively charged environment which interrupts viral synthesis. The CDR also stiffens the membrane of the cell to stop pathogens from exiting it and warns other cells of the danger and emits ATP in order to warn other cells to get their defenses up.